

Q1
to 600 of the sequence set out in Figure 3 (SEQ ID NO:3) or at least nucleotides 1 to 966 of the sequence set out in Figure 5 (SEQ ID NO:5) encodes a 5'-truncated polypeptide, designated PDGF-D (formally designated "VEGF-G"), while at least nucleotides 176 to 1285 of the sequence set out in Figure 7 (SEQ ID NO:7) encodes a full-length PDGF-D. The sequence of at least nucleotides 1 to 1110 of SEQ ID NO:35 encodes a murine PDGF-D, while the sequence of at least nucleotides 1-1092 of SEQ ID NO:37 encodes an identical protein as SEQ ID NO:35 except for a six amino acid residue gap (a.a. #42-47) from the region between the signal sequence and the CUB domain (see below for details) , and SEQ ID NO:39 a C-terminal truncated protein of the polypeptide encoded by SEQ ID NO:35. The PDGF-D polynucleotide of the invention can be a naked plynucleotide and/or in a vector or liposome.

Please amend Paragraph [0036] as follows:

Q2
[0036] PDGF-D is structurally homologous to PDGF-A, PDGF-B, VEGF, VEGF-B, VEGF-C and VEGF-D. The sequence of at least nucleotides 935 to 1285 set out in Figure 7 (SEQ ID NO:7) encodes a portion of the PDGF/VEGF homology domain, which is the bioactive fragment of PDGF-D. This bioactive fragment would also be encoded by the sequence of at least nucleotides 1 to 600 of the sequence set out in Figure 3 (SEQ ID NO:3) or at least nucleotides 1 to 966 of the sequence set out in Figure 5 (SEQ ID NO:5).

Please amend Paragraph [0038] as follows:

Q3
[0038] A preferred fragment is a truncated form of PDGF-D comprising a portion of the PDGF/VEGF homology domain (PVHD) of PDGF-D. The portion of the PVHD is from residues 254-370 of Figure 8 (SEQ ID NO:8) where the putative proteolytic processing site RKS^K starts at amino acid residue 254 (SEQ ID NO:8). However, the PVHD extends toward the N terminus up to residue 234 of Figure 8 (SEQ ID NO:8). Herein the PVHD is defined as truncated PDGF-D. The truncated PDGF-D is the putative activated form of PDGF-D.

Please amend Paragraph [0079] as follows:

Q4 [0079] Another aspect of the invention relates to the discovery that the full length PDGF-D protein is likely to be a latent growth factor that needs to be activated by proteolytic processing to release an active PDGF/VEGF homology domain. A putative proteolytic site is found in residues 254-257 in the full length protein, residues -RKS- (SEQ ID NO:9). This is a dibasic motif. The -RKS- (SEQ ID NO:9) putative proteolytic site is also found in PDGF-A, PDGF-B, VEGF-C and VEGF-D. In these four proteins, the putative proteolytic site is also found just before the minimal domain for the PDGF/VEGF homology domain. Together these facts indicate that this is the proteolytic site.

Please amend Paragraph [0092] as follows:

Q5 [0092] Figure 7 (SEQ ID NO:7) shows the complete nucleotide sequence of cDNA encoding a hPDGF-D(1116 bp) and the deduced amino acid sequence of full-length hPDGF-D encoded thereby which consists of 370 amino acid residues (Figure 8-SEQ ID NO:8);

Please amend Paragraph [00123] as follows:

Q6 [00123] The N-terminal region of the partial PDGF-D amino acid sequence of Figure 12 (residues 53-170 of SEQ ID NO:8) has a second distinct protein domain which is referred to as a CUB domain (Bork and Beckmann, J. Mol. Biol., 1993 231, 539-545). This domain of about 115 amino acids was originally identified in complement factors C1r/C1s, but has recently been identified in several other extracellular proteins including signaling molecules such as bone morphogenic protein 1 (BMP-1) (Wozney *et al.*, Science, 1988 242, 1528-1534) as well as in several receptor molecules such as neuropilin-1 (NP-1) (Soker *et al.*, Cell, 1998 92 735-745). The functional roles of CUB domains are not clear but they may participate in protein-protein interactions or in interactions with carbohydrates including heparin sulfate proteoglycans. These interactions may play a role in the proteolytic activation of PDGF-D.